Catalytic oxidations by vanadium complexes

Ligtenbarg, A.G J; Hage, R.; Feringa, B.L.

Published in:
Coordination Chemistry Reviews

DOI:
10.1016/S0010-8545(02)00308-9

Publication date:
2003

ELSEVIER

Coordination Chemistry Reviews 237 (2003) 89–101

COORDINATION CHEMISTRY REVIEWS

www.elsevier.com/locate/ccr

Catalytic oxidations by vanadium complexes

Alette G.J. Ligtenbarg [a], Ronald Hage [b], Ben L. Feringa [a,*]

[a] *Laboratory of Organic Chemistry, Strating Institute, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands*
[b] *Unilever Research Laboratory Vlaardingen, PO Box 114, 3130 AC Vlaardingen, The Netherlands*

Received 25 January 2002; accepted 13 November 2002

Contents

Abstract

Vanadium haloperoxidases catalyse the oxidation of halides leading to halogenation of substrates or, in the absence of suitable substrates, to oxidation of hydrogen peroxide into singlet oxygen and water. Furthermore, V-haloperoxidases are capable to give enantioselective sulfoxidation under the appropriate conditions. The most interesting model compounds that have been synthesised and studied as bromination catalysts, and catalysts for, i.e. epoxidation, hydroxylation, sulfoxidation and alcohol oxidation are discussed in this paper. Our recent work includes the investigation on a vanadium complex as potential catalyst for bromination reactions, attempts to synthesise a novel structural model for the active site of V-peroxidase using a tripodal ligand, and the syntheses and characterisation of four new vanadium complexes containing tridentate ligands. The latter compounds have been studied as oxidation catalysts using cinnamyl alcohol as substrate.

Keywords: Vanadium; Catalyst; Catalytic oxidation; Ligand; Biomimetic oxidation; Bromination

1. Vanadium haloperoxidase enzymes

Haloperoxidases are enzymes that catalyse the oxidation of halides to the corresponding hypohalous acids or to a related two-electron oxidised halogenating intermediate such as OX^-, X_3^- and X^+, using hydrogen peroxide as the oxidant. Various types of haloperoxidases exist, like iodoperoxidases (catalyse the oxidation of iodide), bromoperoxidases (catalyse the oxidation of bromide and iodide) and chloroperoxidases (catalyse the oxidation of chloride, bromide and iodide). In the presence of suitable nucleophilic acceptors, halogenated compounds are formed [1,2]. These products probably are formed because of the biocidal effects of HOBr and some of the organohalogens. Presumably, these compounds are part of the host defence system, because they may prevent fouling by microorganisms or act as an antifeeding system [3].

* Corresponding author. Tel.: +31-503-634-278; fax: +31-503-634-296
E-mail address: feringa@chem.rug.nl (B.L. Feringa).

0010-8545/02/$ - see front matter
PII: S0010-8545(02)00308-9

Vanadium peroxidases, found in red and brown seaweeds or terrestial fungi, have been shown to catalyse the bromination of various organic substrates including 2-chloro-5,5-dimethyl-1,3-cyclohexane-dione (mcd), the standard substrate for the determination of haloperoxidase activity using H_2O_2 as the oxidant [4]. In the absence of a nucleophilic acceptor, however, a second equivalent of hydrogen peroxide reduces the brominating intermediate resulting in the formation of bromide and singlet oxygen [5]. This disproportionation reaction of hydrogen peroxide is a bromide-mediated reaction, i.e. V–BrPO does not catalyse the formation of singlet oxygen in the absence of bromide. As an example, at pH 6.5 using 2 mM hydrogen peroxide, 0.1 M bromide and 50 μM mcd, the specific activity of *Ascophyllum nodosum* towards bromination of mcd is 170 U mg^{-1} [6]. A common intermediate ('Br^+') is likely to exist of which the formation is rate determining and which is responsible for both the generation of singlet dioxygen and brominated products (see Fig. 1). Nevertheless, the exact nature of this halogenating intermediate has not been determined as yet.

In the past many spectroscopic studies have been carried out in order to reveal the nature of the active site and the mechanism of action. Investigations concerning the coordination environment around vanadium were performed on the native enzyme as well as on the reduced V(IV) form e.g. using X-ray absorption measurements, EPR spectroscopy, and ^{51}V-NMR spectroscopy [6].

In 1996, the crystal structure of an azide containing vanadium chloroperoxidase (V–ClPO) isolated from the

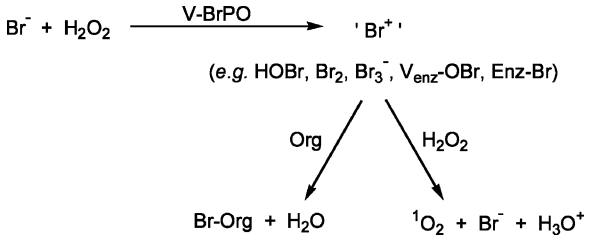


Fig. 1. Proposed mechanism of bromoperoxidase activity catalysed by V–BrPO [5].

fungus *Curvularia inaequalis* was determined by Messerschmidt and Wever [7], whilst the X-ray of the peroxo adduct of chloroperoxidase was published a year later [8]. In the native state, a five-coordinated trigonal bipyrimidal V(V) moiety is present which is coordinated by three nonprotein oxo groups in the equatorial plane and one histidine and a hydroxy group at the axial positions (Fig. 2). Two X-ray structures from the seaweed enzymes *Corallina officinalis* and *A. nodosum* have also been published [9,10].

The oxygen donors bound to the vanadium ion are hydrogen bonded to several amino acid residues of the protein chain. In the peroxo state, the peroxide ligand is bound in an μ^2-manner in the equatorial plane. The coordination geometry around the vanadium centre is a distorted tetragonal pyramid with the two peroxo oxygens, one oxygen and the nitrogen in the basal plane and one oxygen in the apical position. A partial amino acid sequence comparison of this chloroperoxidase with a vanadium bromoperoxidase showed a close similarity between the enzymes [7].

Based on a variety of studies, a mechanism as depicted in Fig. 3 has been proposed [8]. The apical hydroxy unit is hydrogen bonded to a histidine residue (His_{404}) in a protein environment. This hydrogen bond makes the HO^- group more nucleophilic. When a peroxide molecule approaches the active site, the HO^- unit is protonated and HOO^- is generated. The weakly ligated water molecule dissociates from the vanadium ion and a side-on bound peroxide intermediate is formed after the departure of another water molecule. Subsequently, attack of a chloride ion at one of the peroxo atoms and the uptake of a proton from a surrounding water molecule leads to the generation of hypochlorous acid (HOCl) and restoration of the native state.

At higher acid concentrations, the halogenation activity was inhibited. It was assumed that this is due to protonation of His_{404}. As a result, the formation of the peroxide form does not occur, since it is now impossible for the histidine residue to form a hydrogen bond to the apical OH group. As a consequence, this hydroxy unit loses its ability to activate the H_2O_2 by

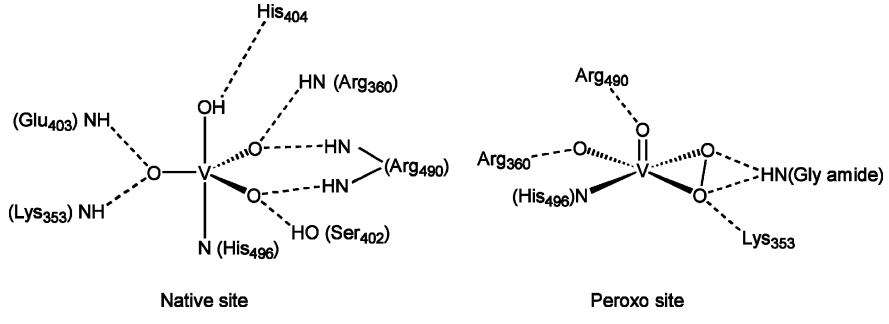


Fig. 2. The native and peroxo vanadium site in V–ClPO [7,8].

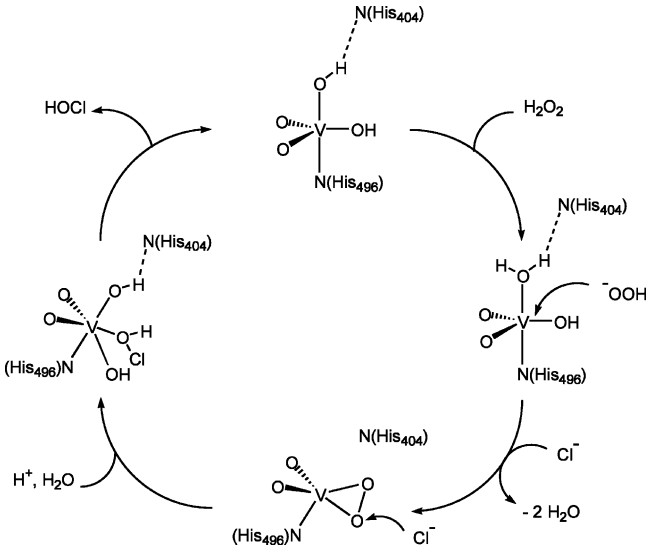


Fig. 3. Proposed catalytic mechanism of V–ClPO.

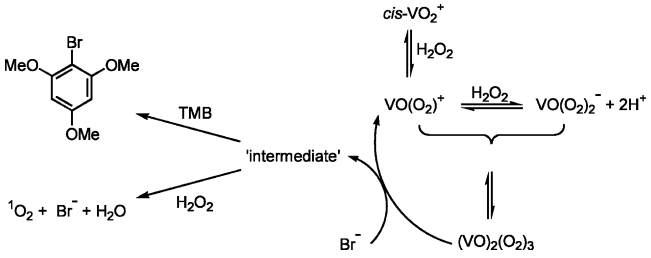


Fig. 4. Bromination activity of the V–BrPO mimic *cis*-dioxovanadium(V) [11].

deprotonation and, therefore, the peroxide can not be bound to the vanadium ion.

2. Functional models of V-haloperoxidases

A variety of vanadium compounds have been studied as functional models for V-haloperoxidases to get a better understanding of the working mechanism of the vanadium haloperoxidase enzyme and to determine the role of vanadium [6]. Some examples will be given in this paper.

The first reported functional mimic of V–BrPO is *cis*-dioxovanadium(V) (VO_2^+) in acidic aqueous solution [11,12]. *Cis*-dioxovanadium(V) is shown to catalyse the bromination of 1,3,5-trimethoxybenzene (TMB) as well as the bromide-mediated disproportionation of H_2O_2. In a first step, H_2O_2 is complexed giving red oxoperoxo $[VO(O_2)]^+$ and yellow oxodiperoxo $[VO(O_2)_2]^-$ complexes. The ratio between these two species depends on the H_2O_2 concentration and the pH. In a second step these species combine, yielding dioxotriperoxodivanadium(V) $[(VO)_2(O_2)_3]$, which is considered to be the actual oxidant (Fig. 4). Contrary to natural haloperoxidases, *cis*-dioxovanadium(V) only functions at low pH (2 or less), because at lower acid concentrations the amount of monoperoxovanadate is insufficient for dimerisation to occur to $[(VO)_2(O_2)_3]$. Another difference with the enzyme is the low rate of catalysis indicating the importance of the protein environment around the active site.

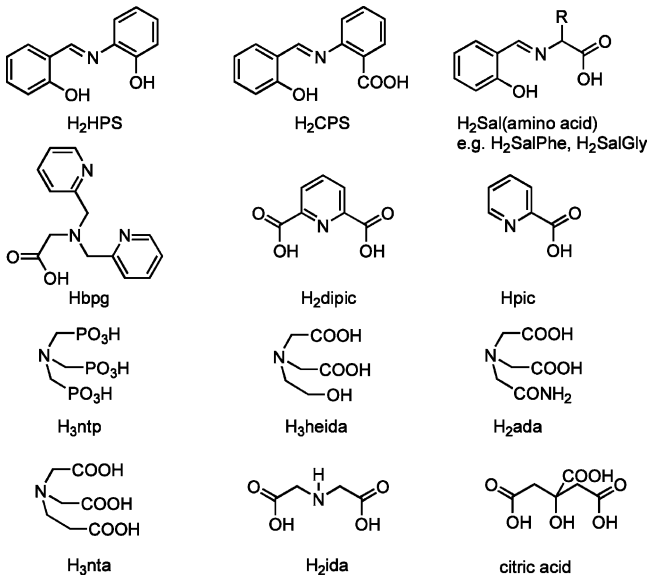


Fig. 5. Ligands whose V(V) complexes have been tested for catalysis of bromide oxidation [6].

In recent years several vanadium complexes of multidentate ligands containing O and N donor sites (depicted in Fig. 5) were tested for catalysis of bromide oxidation [6]. Ligands that yield active functional model systems for V–BrPO include Schiff base ligands derived from salicylideneamino acid (H_2SalPhe, H_2SalGly) [13,14] an imine of salicylaldehyde (H_2HPS) [15], iminodiacetic acid (H_2ida) [16,17], nitrilotriacetic acid (H_3nta) [16,17], citric acid [18] and various tripodal amine ligands (H_3heida, H_2ada, Hbpg) [16,17]. When the vanadium(V) peroxo adduct becomes too much stabilised by the donating properties of the ligand, as for instance observed for pyridine-2,6-dicarboxylic acid (H_2dipic), oxidation of bromide is not observed.

Also various complexes have been published that are not stable under the applied reaction conditions. Examples include the corresponding vanadium(V) compounds of carboxyphenylsalicylideneamine (H_2CPS), pyridine-2-carboxylic acid (Hpic), and nitrilotriphosphoric acid (H_3ntp) [6,18,19]. These ligands dissociate from the metal ion in the presence of acid and H_2O_2.

A V–BrPO mimic that has been well studied is the oxovanadium(V) complex of hydroxyphenyl-salicylideneamine [(HPS)VO(OEt)(EtOH)] (Fig. 6) [20]. The bromination experiments with [(HPS)VO(OEt)(EtOH)] are performed in DMF solution. Several vanadium species are formed as was identified by ^{51}V-NMR

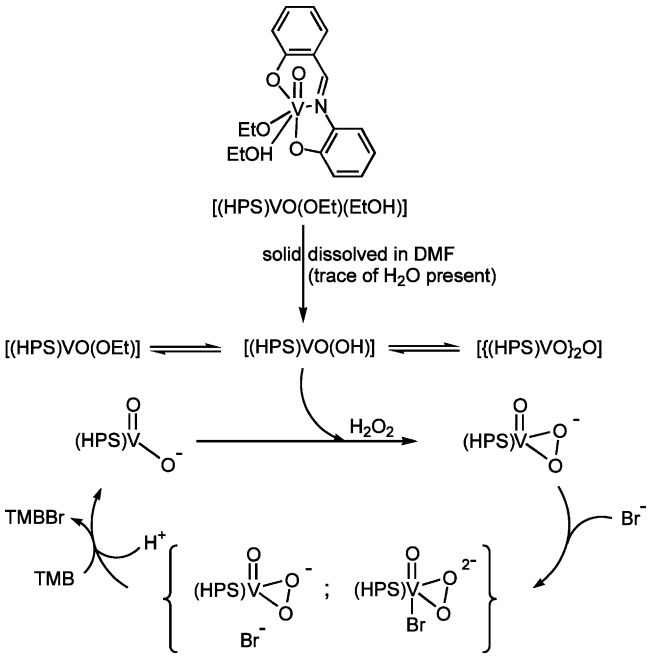


Fig. 6. Proposed mechanism for bromide oxidation by H_2O_2 catalysed by (HPS)VO(OH) [20].

spectroscopy. Upon addition of H_2O_2, a single oxoperoxovanadium(V) complex $[(HPS)VO(O_2)]^-$ is formed. Subsequently addition of bromide affords one turnover towards a two-electron oxidised form (e.g. HOBr, Br_2, Br_3^-, or V–OBr), which in the presence of trimethoxybenzene (TMB) yields one equivalent of the brominated product 2-bromo-1,3,5-trimethoxy-benzene (TMBBr). It is still not clear whether the Br^- is bound directly to vanadium, which is then followed by oxidation by the vanadium peroxo complex, or that there is a nucleophilic attack by Br^- on the coordinated peroxide, giving rise to bound ^-OBr. The formed intermediate, however, is subject to rapid equilibration with HOBr, Br_2, and Br_3^-, since the presence of Br_3^- was spectroscopically established. The bromination reaction becomes catalytic when acid is used in at least stoichiometric quantities with respect to H_2O_2.

Other examples of well-studied V–BrPO mimics are several vanadyl $[V(IV)O]^{2+}$ complexes with oxalate, glutarate, succinate, malonate, and acetate ligands by Sakurai and Tsuchiya [21]. The mechanism proposed includes the formation of a V(IV) intermediate, which is distinct from the mechanism proposed for vanadium haloperoxidases, based on the absence of EPR signals corresponding to V(IV) species.

3. Haloperoxidase activity using a vanadium diamidate complex

In the literature, several vanadium complexes with amidate ligands are known which are used as model systems to study vanadium–protein interactions [22–26]. However, no reports on these type of compounds as mimics for V–BrPO have been found. Therefore, we prepared the vanadium(IV)–hybeb complex synthesised before by Keramidas et al. [22] and tested it as a catalyst in the bromination reaction of trimethoxybenzene. The ligand H_4L^1 (1,2-bis(2-hydroxybenzamido)benzene Fig. 7) [22] was reacted with vanadyl acetyl acetone in the presence of two equivalents of sodium hydroxide under an argon atmosphere, yielding the desired V(IV) complex. Reaction with $AgNO_3$ in acetonitrile yields the analogous V(V) complex [22].

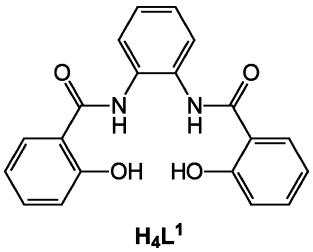


Fig. 7. Structure of H_4 L^1.

The ^1H and ^{51}V-NMR spectrum recorded in dimethylformamide-d_7 are in agreement with the one reported [22] with this assignment, since no phenolic or amidate hydrogens were observed [22]. The UV spectra of the vanadium(IV) and vanadium(V) complexes were also in agreement with those published [20]. The electrospray mass spectra of these compounds were not published elsewhere and some results are given in this contribution. The negative electrospray mass (ES-MS) spectrum of $[(L^1)V(IV)=O]^{2-}$ recorded in acetonitrile showed peaks at *m/z* 206, 412, and 434, which correspond to $\{[(L^1)V(IV)O]^{2-}\}$, $\{[(L^1)V(IV)O]^{2-}+1H^+\}$ and $\{[(L^1)V(IV)O]^{2-}+1Na^+\}$, respectively. However, the positive ion spectrum recorded in MeOH showed major peaks at *m/z* 457, 480, and 413 which are attributed to $\{[(L^1)V(V)O]^-+2Na^+\}$, $\{[(L^1)V(IV)O]^{2-}+3Na^+\}$ and $\{[(L^1)V(V)O]^-+2H^+\}$. Under these conditions, the vanadium(IV) ion is oxidised to V(V) under these conditions, in agreement with the reported synthesis of the vanadium(V) species with the same ligand [22]. The ES-MS spectrum of the oxidised analog recorded in acetonitrile shows one parent peak at *m/z* 411 which can be assigned to $\{[(L^1)V(V)O]^-\}$.

In order to examine halide oxidation catalysed by the vanadium(IV)–L^1 complex, we have used trimethoxybenzene as model substrate (TMB) [11,16,17]. Hydrogen peroxide (30% in water) was used as the oxidant and tetrabutylammonium bromide (Bu_4NBr) as the bromide source. Dimethylformamide was used as the solvent, since we found that in that case only 2-bromo-1,3,5-trimethoxybenzene [TMBBr] was obtained. When, e.g. a mixture of EtOAc and DMF was used, dibrominated 2,4-bromo-1,3,5-trimethoxybenzene [$TMBBr_2$] was

formed as well. In a typical experiment, 10 mM of TMB and 50 mM of Bu_4NBr were used. The reactions were performed under an argon atmosphere because it is known that the complex is hydrolysed when both water and air are present [22]. The progress of the reaction was monitored by GC. The addition of acid (HCl) was necessary for the reaction to proceed (vide infra). No chlorination products were observed. Some of the results are summarised in the table below (Table 1). As reference, we have used vanadium–acetylacetonate and the well-studied V–HPS complex [20], as well as the blank (no vanadium complex present).

In all cases, the only observed product was 2-bromo-1,3,5-trimethoxybenzene (TMBBr). When 0.25 mM of catalyst was applied, $VO(acac)_2$ proved to be inferior to the other two catalysts. When after 2 h an additional amount of H_2O_2 was added to the $VO(acac)_2$ system, the conversion increased from 3.8 to 4.5 mM TMBBr, whereas in the other cases the amount of product remained nearly the same. Preliminary experiments using the $V(V)O(L^1)$ complex as the catalyst show similar results as for vanadium(IV) analog. It is noteworthy to observe that the blank (no vanadium present in the solution) yields a significant conversion of the substrate as well, although in the first 30 min the conversion is significant less than observed for the vanadium complexes.

In order to study the species involved in the catalytic TMB oxidation process, we have conducted UV–vis and NMR measurements in DMF. The stability of the V(IV) complex in the presence of H_2O_2 was investigated using ^{51}V-NMR measurements. As the vanadium(IV) complex itself is paramagnetic, no signal was observed but after addition of H_2O_2, one peak at -726 ppm (b.w. = 258 Hz) appeared in CD_3CN. This signal was attributed to a peroxodiamidatevanadium(V) species, since it is known that often a signal for (diperoxo)vanadium(V) arises at -585 ppm when the ligand dissociates from the metal [18]. Even after 30 min, the formation of dissociation products was not detected, suggesting that the complex remains intact under the applied reaction conditions. These findings were corroborated by the UV–vis spectroscopic measurements, as only very slowly (24 h) full dissociation of the ligand was observed. These results show that, in contrast to water [22], the $V–L^1$ complex in the presence of hydrogen peroxide is quite stable. As shown above, in order to yield bromination an excess of hydrochloric acid needed to be added, and under these conditions we have observed using UV–vis, immediate formation of uncoordinated H_4L^1. These findings suggest that the observed catalysis is presumably accomplished by the generated vanadium(V) species that is not ligated to the L1 ligand. Preliminary ^{51}V-NMR measurements with the $V(V)L^1$ complex in the presence of excess H_2O_2 in CD_3CN suggest that $[(VO)_2(O_2)_3]$ may be responsible for the catalytic activity, because a resonance at -670 ppm (b.w. = 361 Hz) is observed after a few minutes. This signal was attributed to the binuclear oxovanadium(V) triperoxo species $[(VO)_2(O_2)_3]$ by comparison with literature data [19] The bromination activity using the $V(IV)–L^1$ and $V(V)–L^1$ complexes is identical, which suggests that the catalysis is achieved by the same vanadium species. Although this signal was not observed in the ^{51}V-NMR spectrum of the vanadium(IV)–L^1 complex and H_2O_2, presumably due to trace levels of the paramagnetic residual V(IV) species, it is highly conceivable that after addition of acid also in this case the triperoxo species is formed. These results are in contrast to the [(HPS)VO(OEt)(EtOH)] system, which has been shown by using UV–vis and ^{51}V-NMR spectroscopies to yield catalysis with the HPS ligand bound to the vanadium ion [20].

A problem with the bromination reactions using TMB as the substrate is the relatively fast blank reaction in acidic media. Further, the studies using vanadium complexes as bromination catalysts showed that bromination of TMB only takes place at low pH, therefore, the blank reaction is high and these harsh reaction conditions may easily cause the dissociation of the ligand. It appears that only ligands containing two or three negatively charged oxygen donor atoms yield vanadium complexes, that are likely to be stable under the reaction conditions. Although the $V–L^1$ compounds and the vanadium complex with [H_2CPS] [15] fulfil these requirements, they dissociate upon addition of H_2O_2 and acid. On the other hand, the tripodal amine ligand [Hbpg] which contains two pyridine nitrogen donors and only one anionic oxygen donor atom, proved to be an active functional bromoperoxidase mimic [16,17]. Thus, it appears that predicting stability and activity of new vanadium model complexes is still a difficult task. It can, therefore, be concluded that the search for a ligand system that provides a robust catalyst capable of approaching the enzyme in reaction rate and selectivity remains a challenge.

Table 1
Bromination of TMB by $[VO(L^1)]Na_2$ [22], [(HPS)VO(EtO)(EtOH)]—denoted as (HPS)VO [20] and $VO(acac)_2$

	[TMBBr] 0.5 h	[TMBBr] 1 h	[TMBBr] 2 h
$VO(L^1)$	4.8	6.2	6.2
(HPS)VO	5.1	7.7	7.9
$VO(acac)_2$	3.6	3.7	3.8
No catalyst	1.8	n.d.	3.5

Conditions: 10 mM TMB, 10 mM H_2O_2, 8 mM HCl, 0.25 mM V-complex and 50 mM tetrabutylammonium bromide in DMF.

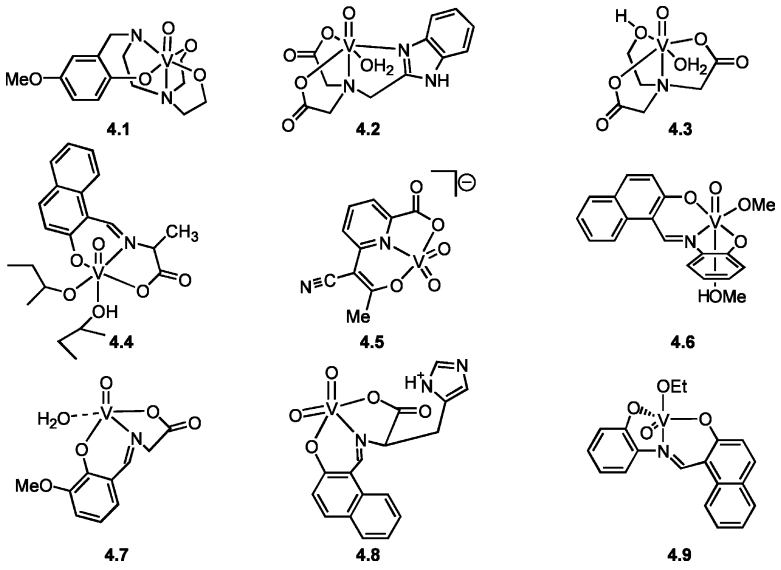


Fig. 8. Structural models for the active site of vanadate-dependent haloperoxidases [27].

4. Design of a structural model of vanadium-haloperoxidases

As mentioned above, the structure of vanadium haloperoxidase shows that the vanadium ion is ligated to the protein backbone via one histidine nitrogen donor, whilst the oxo moieties are strongly H-bonded to arginine, lysine, histidine and serine amino acids [6] (see Fig. 2 for a schematic representation).

Apart from the functional models as described in the previous section, various model systems were also designed in order to examine which structural features are important for the catalytic properties of these enzymes [27,28] A selection of these compounds is depicted in Fig. 8.

Vanadium is either in the +4 oxidation state (4.2 [29], 4.3 [30] and 4.7 [31]) or the +5 state (4.1 [32], 4.4 [33], 4.5 [34], 4.6 [31], 4.8 [35], 4.9 [31]). All ligands contain oxygen donor sites and often one or two oxo groups are present at the vanadium centre. The non-oxo oxygens stem from alkoxide and phenolate moieties or from a water molecule. Compound 4.2 exists of an benzimidazol unit incorporated in the ligand system, thus providing a model for the coordination of histidine in the enzyme [29]. In some of the complexes, one of the vanadium-to-oxygen linkages is a weak bond, for instance when water (4.3 and 4.7) or an alcohol (4.4 and 4.6) coordinate to the metal. These bonds may easily dissociate to provide an additional coordination site for a substrate.

As shown in Fig. 8, the structural models known to date mimic the oxygen-rich coordination environment of the metal and the binding of histidine in the presence of oxo groups, phenolate and alkoxide moieties, and one nitrogen donor unit. However, none of these structures display the characteristic hydrogen bonding pattern of the oxo groups on vanadium to other residues present in the ligand. Therefore, the design of a structural mimic in which the vanadate (VO_3^-) moiety is coordinated to a nitrogen donor atom and stabilised via hydrogen bonds to other parts of the ligand, remains to be achieved. Recently the synthesis of a polyamine receptor ligand containing two guanidinium units and an imidazole ligand as a template suitable to bind vanadate via hydrogen bridges was reported (Fig. 9) [36]. This ligand was designed according to the structural properties known from the X-ray crystal structure from vanadium chloroperoxidase. The bisguanidinium moieties were chosen taking into account the well-established recognition of phosphate by these type of receptors. The structure of the corresponding vanadate complex is not published yet.

Another ligand that can provide hydrogen bonds is the tripodal ligand, depicted in Fig. 10, developed by

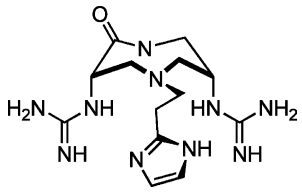


Fig. 9. Bisguanidinium receptor ligand for the incorporation of vanadate [36].

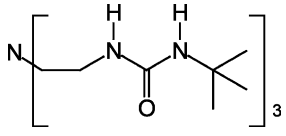
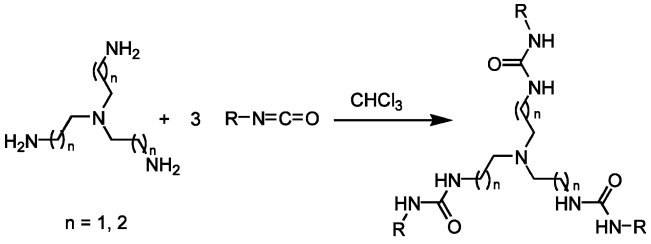


Fig. 10. Urea based tripodal ligand studied by Borovik and co-workers [37,38].

Borovik and coworkers. With this ligand a variety of Mn, Fe, and Co complexes have been studied [37,38]. This tripodal urea-based ligand affords a cavity structure that incorporates the metal and the additional hydroxo or oxo group on the metal is stabilised by the hydrogen bonds.

One of the tripodal urea compounds, L^2 has been reported as a receptor for phosphate [39]. An association constant (K_{ass}) of $1.1 \times 10^4\ M^{-1}$ was obtained with tris(tetra-methylammonium)phosphate in DMSO-d_6. Since physiological effects of vanadium are mainly attributed to the similarity of vanadate(V) ions and phosphate ions [40] and because it was recently discovered that the active sites of vanadate containing haloperoxidases and of families of acid phosphatases are very similar [41], it was envisaged that this tripodal ligand is also capable of coordination of vanadate in a similar manner.

To study the possibilities of these types of tripodal urea-based compounds as ligands for vanadate, five derivatives were synthesised. Reaction of tris(2-aminoethyl)amine with phenyl, butyl, or benzyl isocyanate in chloroform afforded L^2, L^3 and L^4, respectively, in good yields (Fig. 11). Although tris(2-aminoethyl)amine



Compound	Spacer	R	Yield (%)
L^2	C_2	Phenyl	96
L^3	C_2	Butyl	75
L^4	C_2	Benzyl	71
L^5	C_3	Butyl	82
L^6	C_3	Benzyl	91

Fig. 11. Synthesis of tripodal ligands [42,43].

appeared to be a suitable spacer for a phosphate receptor, also two ligands based on the C3-spacer tris(3-aminopropyl)amine were prepared for the purpose of comparison (L^5 and L^6).

In order to achieve incorporation of the vanadate ion into the ligand cavity, tetra-*n*-butylammonium vanadate was used, which was prepared via a slightly modified literature procedure from vanadium pentoxide (V_2O_5) and a 0.4 M solution of $[(^nBu)_4N]OH$ in water [44]. The target structure based on ligands L^5 or L^6 is depicted in Fig. 12.

In the first attempts to synthesise the target molecule, ligands L^2–L^6 were mixed with $[(^nBu_4N)VO_3]$ in a 1:1 ratio using DMA (*N*,*N*-dimethylacetamide) as the solvent. After slow diffusion of diethyl ether into the solution, purple crystals were obtained in all cases. However, ^{1}H-NMR revealed that the ligands were absent in the compound. According to the elemental analysis, probably a tetra-*n*-butylammonium hydrogen divanadate complex $[(^nBu_4N)HV_2O_6]$ was formed. Also addition of ethylacetate, benzene and diisopropylether yielded these purple crystals. When the reaction was performed in octanol only starting material (the ligand or the vanadium reagent) could be isolated after slow addition of diethyl ether or evaporation of the solvent.

The association constant (K_{ass}) of ligand L^2 with phosphate was determined in DMSO-d_6 [39]. Accordingly, concentration dependent ^{51}V-NMR experiments were performed in this solvent using ligand L^4 and $[(^nBu_4N)VO_3]$, in a 1:1 ratio. The vanadium reagent exhibits a signal at -570 ppm and addition of the ligand had no influence on this value. Subsequently dilution of the sample also did not produce a concentration dependent shift, indicating that coordination of the vanadate moiety does not occur.

Since the tripodal ligands, insoluble in acetone, readily dissolve by addition of excess $[(^nBu_4N)VO_3]$, it was assumed that in acetone perhaps coordination of the vanadate moiety to the urea groups occurs. Therefore, ^{51}V-NMR studies in acetone-d_6 were performed using the vanadium reagent and ligand L^5. A single resonance at -564 ppm was detected for $[(^nBu_4N)VO_3]$. Unfortunately, this remained the same after addition of the ligand, which implies that incorporation of vanadate into the triurea compound via hydrogen bonding does not occur. We have not performed further studies to

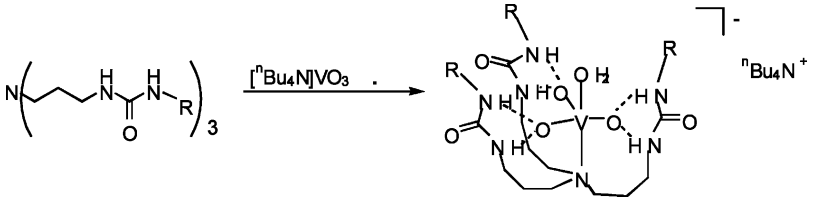


Fig. 12. Target structural model system of vanadium bromoperoxidase using tripodal ligand L^5 or L^6.

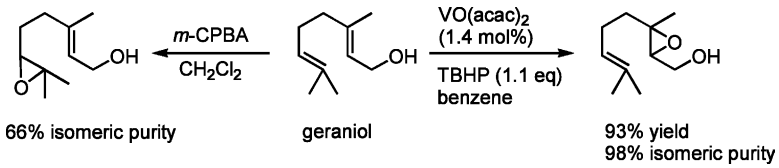


Fig. 13. Epoxidation of geraniol catalysed by $VO(acac)_2$ and TBHP or *m*-CPBA.

understand why the vanadate ion does not appear to bind unlike the phosphate anion [39].

5. Vanadium complexes for oxidation catalysis

As a consequence of their low radius/charge ratio, vanadium(V) centres are usually strong Lewis acids, which makes them suitable for the activation of peroxidic reagents [45]. Accordingly, vanadium(V) complexes have been found to act as catalyst precursors in various oxidation reactions like bromination reactions, epoxidations of alkenes and allylic alcohols, oxidations of sulfides to sulfoxides and sulfones, hydroxylations of alkanes and arenes, and oxidations of primary and secondary alcohols to the corresponding aldehydes and ketones [46]. Examples of these types of oxidations will be discussed below. The active species has been identified in stoichiometric reactions as mononuclear oxoperoxovanadium(V) complexes, some of which have been structurally characterised [47]. In all cases the peroxide is bound in an η^2-manner in the equatorial plane relative to the axial oxo ligand. Vanadium(IV) complexes can also be used as precursors in these oxidation reactions. In the presence of excess peroxide, they are readily converted to the oxoperoxovanadium(V) complexes [46].

Simple vanadium complexes, e.g. vanadyl acetylacetonate $[VO(acac)_2]$, are useful catalysts in the epoxidation of allylic alcohols. The actual oxoperoxo catalyst is formed in situ by oxidation of V(IV) to V(V) with excess of alkylhydroperoxide, yielding an alkylhydroperoxo vanadium(V) complex [48]. An excellent example of high regioselectivity is the epoxidation of geraniol catalysed by a $VO(acac)_2$–TBHP (*tert*-butylhydroperoxide) system. The allylic double bond is selectively oxidised, whereas peracids preferentially epoxidise the isolated double bond [49,50] (Fig. 13).

Several vanadium complexes are known to catalyse the oxidation of unfunctionalised olefins [47,51]. It was proposed that when a vacant site on the vanadium centre is present, the olefins are able to coordinate to the vanadium centre, leading to the formation of epoxides with high selectivity [52]. However, when coordination of the olefin is not possible, one-electron oxidation processes often play a role, which proceed in a non-stereoselective manner.

Simple vanadium(V) peroxide complexes also are efficient and selective catalysts in the oxidation of prochiral dialkyl, arylalkyl or diaryl sulfides to the corresponding sulfoxides. These complexes are usually generated in situ from vanadium salts such as $VO(acac)_2$, sodium *meta*-vanadate ($NaVO_3$), or vanadium pentoxide (V_2O_5) and H_2O_2. The reactions are often nearly quantitative with respect to the peroxide. Two mechanisms may occur, dependent on the nature of the ligand [53]. The reaction pathway proceeds either via heterolytic or homolytic cleavage of the peroxidic oxygen–oxygen bond. For example, $VO(O_2)(OCH_3)$ oxidises di-*n*-butyl sulfide as well as methyl phenyl sulfide in a bimolecular, electrophilic reaction. In the proposed mechanism the sulfide does not coordinate to the metal centre, but undergoes nucleophilic addition to the peroxide oxygen, i.e. the oxygen is electrophilic in nature (Fig. 14). This mechanistic route is common for peroxometal complexes such as Ti(IV) and Mo(VI) derivatives [51].

The electrophilic or nucleophilic character of the peroxide oxygen transfered to the sulfide can be established by using thianthrene 5-oxide (SSO) as a mechanistic probe (Fig. 15) [54]. This compound has both a sulfide and a sulfoxide site. The electron-rich sulfide is expected to undergo preferably electrophilic oxidation giving SOSO, whereas the more electron

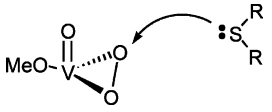


Fig. 14. Nucleophilic addition of a sulfide to the peroxide oxygen of $VO(O_2)(OCH_3)$.

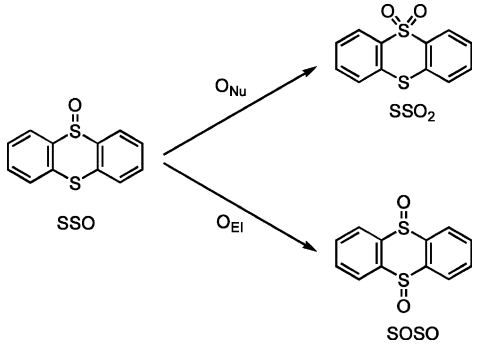


Fig. 15. Reaction of thianthrene 5-oxide (SSO) with nucleophilic and electrophilic peroxide species.

deficient sulfoxide sulfur is expected to undergo nucleophilic oxidation yielding SSO_2. Consequently, those oxidants that give high amounts of SOSO product are electrophilic in their reactivity, while high yields of sulfone point to a nucleophilic oxidant.

Given the electrophilic nature of the $VO(O_2)(OCH_3)$ catalyst, the preference for sulfide oxidation over sulfoxide oxidation is obvious. This explains the quantitative yields of sulfoxide found in sulfide oxidation reactions. However, a peroxovanadium(V) complex of picolinic acid, for example, shows low selectivity in sulfide oxidation leading to mixtures of sulfoxides and sulfones. It was proposed that the ligand suppresses the rate of the heterolytic reaction by reducing the electrophilicity of the peroxo oxygen. Here, a competitive homolytic pathway is likely to occur via one-electron transfer of the bound sulfide, forming a radical cation-radical anion pair (Fig. 16) [55].

The hydroxylation of aromatic hydrocarbons to the corresponding phenolic compounds forms another type of reaction that peroxovanadium(V) complexes are able to catalyse [56,57] Aliphatic hydrocarbons are also hydroxylated, though less easily than arenes, giving alcohols and ketones as the reaction products [58,59]. Further, vanadium(V) peroxo complexes are known to catalyse the oxidation of primary and secondary alcohols to aldehydes and ketones [60]. For instance, vanadium(V) oxytriisopropoxide, $VO(O^iPr)_3$, catalyses the oxidation of 2-propanol by H_2O_2 to acetone. Similarly, ethanol is oxidised to acetaldehyde [59,61].

6. Reactivity of vanadium with a novel Schiff base ligand

As discussed in the previous section, vanadium complexes with Schiff-base ligands were found to give active catalysts for bromination of substrates. The ligand depicted in Fig. 17, (2-hydroxybenzylidene)di(pyridin-2-yl)methylamine (HL^7), has been synthesised in our laboratory and seemed suitable for the synthesis of a dioxovanadium(V) complex, which would be potentially interesting as oxidation catalyst.

As reported elsewhere [62], reaction of this ligand with $VO(^iOPr)_3$ two different vanadium compounds, depending on the reaction conditions (Fig. 18). Reacting the ligand with vanadium at room temperature under argon yielded the $[L^7VO_2]$ complex, whilst under reflux in the

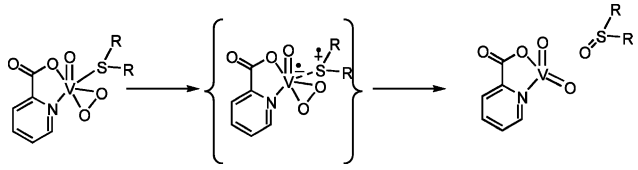


Fig. 16. Radical mechanism for the sulfide oxidation catalysed by $VO(O_2)(pic)$.

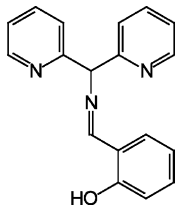


Fig. 17. Structure HL^7.

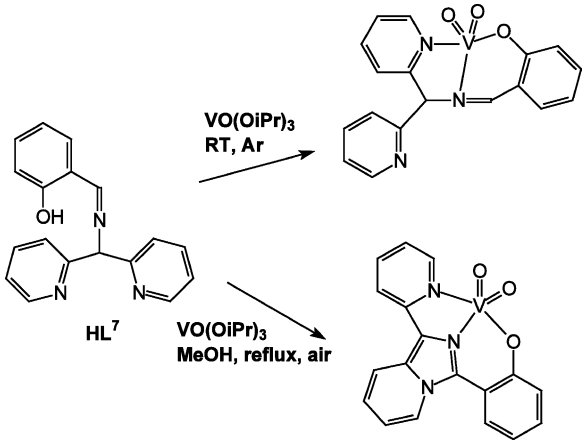


Fig. 18. Synthesis of two vanadium complexes with the Schiff-base ligand HL^7.

air, a cyclisation of the ligand takes place yielding a novel ligand (L^{7A}) bound to the vanadium-dioxo moiety [62]. The latter compound has been characterised using X-ray crystallography, ^{1}H-NMR, ^{51}V-NMR, UV–vis, IR, and electrospray ms measurements [62]. The V–Schiff base complex has not been crystallised, but the other techniques employed unequivocally support the structure as depicted in Fig. 18.

Both complexes were tested as oxidation catalysts, under the conditions as discussed in the previous section on haloperoxidase mimics. Unfortunately, neither of them showed significant activity under the conditions applied. No further studies on the oxidation reactions with these complexes were, therefore, conducted.

7. Vanadium complexes with triazolate ligands

The unusual structure observed for the vanadium complex with L^{7A}, prompted us to study another ligand that has a N_2O donor unit, 3-(2-hydroxyphenyl)-5-(pyridin-2-yl)-1,2,4-triazole-H_2L^8 (see Fig. 19). This

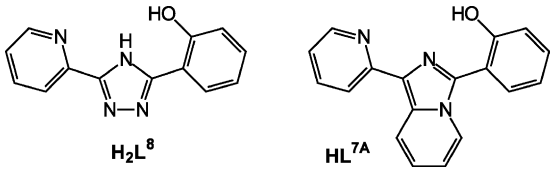


Fig. 19. Structures of $H_2L^8$and HL^{7A}.

ligand has been studied before with ruthenium [63] and like many other triazole ligands, the proton located on the triazole ring becomes easily dissociated upon coordination to the metal ion [64,65]. The properties of the triazolate ligands are distinctively different from the triazole ligands (i.e. undissociated), leading to ruthenium complexes with lower oxidation potentials, lower-energy metal–ligand-charge transfer bands and increased photostability, all due to stronger donating capabilities of the triazolate moiety [65,66]. Therefore, we anticipated that the use of such a ligand would lead to a similar coordination environment as observed for L^{7A}. However, due to increased donating properties of the triazolate ligand, distinct different (catalytic) properties than observed for the V-complex with the imidazo[1,5-a]pyridine type ligand are expected to be present.

The triazole ligand H_2L^8 was treated with sodium metavanadate ($NaVO_3$) in MeOH under an argon atmosphere. The resulting air stable dioxovanadium(V) complex $[VO_2L^8](NH_4)\cdot CH_3CN$, was obtained upon crystallisation from MeOH/Et_2O in the presence of an excess of NH_4PF_6 as yellow needles in 44% yield. In this way, crystals suitable for X-ray analysis were obtained [67]. The structure is very similar to the vanadium compound with the L^{7A}-containing ligand (vide supra), although the V–N4(triazolate) distance is significantly shorter than the distance observed for the V–N(imidazopyridine) bond, in agreement with the increased donating properties of the triazolate ligand.

Interestingly, the reduction potential to the V(IV) species has been observed at a very low potential (−1.65 V vs. ferrocene), in agreement with the strong donating capabilities leading to stabilisation of the high-valent oxidation states. This finding has further corroborated by comparing the UV–vis spectrum of $[VO_2L^8]^-$ with that of $[VO_2L^{7A}]$. The lowest energy LMCT band is at 370 nm, whilst the one for $[VO_2L^{7A}]$ is found at 417 nm, suggesting a significant raise in energy of the empty d-orbital for the $[VO_2L^8]^-$ complex.

A further increase of the donating properties is expected to occur when 3,5-bis(2-hydroxyphenyl)-1,2,4-triazole (H_3L^9) as ligand is employed (see Fig. 20) [67]. Reacting this ligand with $VO(^iOPr)_3$ yielded a dinuclear V(V) complex, in which each vanadium ion is located in a slightly distorted octahedral environment. In the equatorial plane, two phenolic oxygens, the triazole nitrogen atom, and a methoxy group are coordinated to the metal. An oxo group occupies one apical position (V=O bond distances (1.594(4) and 1.597(4) Å)) whereas in the other apical position one phenolic oxygen of the other ligand residue is coordinating (V–O(phenolate): 2.352(3) and 2.314(3) Å) [65]. In this manner a V_2O_2 four-membered ring is formed in which one phenolic oxygen atom of each ligand is bridging between the two metals. Consequently, the other phenolic moiety of the ligand system is bound to one vanadium center. The V···V distance is 3.46 Å.

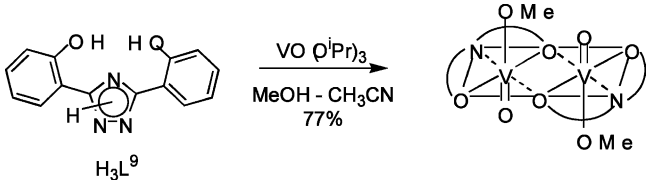


Fig. 20. Synthesis of the dinuclear V complex with H_3L^9.

A similar structure has been observed for bis[2-(2′-hydroxyphenyl)-chinolin-8-olato]dimethoxo-dioxo-divanadium(V) [68]. In this case also, the vanadium ions are surrounded by a methoxy group, an oxo unit, the tridentate ligand, and the bridging phenolate group of the other ligand residue. Also a dinuclear V(IV) complex with phenolate bridges has been recently published; in this case a *N*,*N*-bis(2-hydroxybenzyl) aminoacetic as a ligand has been employed [69].

^{1}H-NMR measurements suggest that the complex dissociates into monomeric species as only one set of aromatic signals is observed in the proton NMR spectrum. If the complex were to exist in the dinuclear structure as depicted in Fig. 19, two sets of resonances of the phenolate moiety were expected to exist. Unfortunately, electrospray ms measurements were not conclusive as both mononuclear (from $\{VOL^9(OMe)-H^+\}$, and dinuclear species (i.e. from $\{(V^{IV}O)(V^{V}O)(L^9)_2(OMe)-1H^+\}$ and $\{(V^{IV}O)_2(L^9)_2(OMe)\}$) were detected using the negative ES-MS mode [67]. A further support for the formation of mononuclear species is obtained from the UV–vis experiments, as the spectrum is reminiscent of the one observed for the $[VO_2L^8]^-$ compound (strong absorption bands at 309 and 390 nm). The electrochemical measurements show again irreversible signals at very negative potentials (−1.72 and −2.16 V vs. ferrocene) [67].

Based on these experiments we cannot positively assign the exact nature of the species, although ES-MS suggested a $[L^9V{=}O(OMe)]^-$ species. If this assignment is correct, the additional charge donated by the bisphenoltriazole ligand is compensated for by the replacement of one oxo group by a methoxide anion, yielding the same charged species. This would explain the observation that the UV–vis bands are not shifted to higher energies, as would be expected when the d-orbital is further raised due to increased donating capabilities of the ligand.

8. Catalytic oxidation reactions using the vanadium complexes with the triazole-based ligands

As explained above, various vanadium compounds give efficient and selective allylic oxidation reactions.

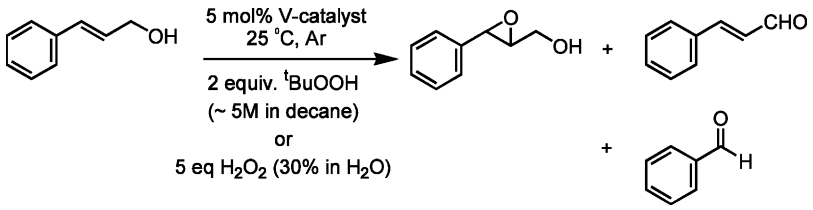


Fig. 21. Catalytic oxidation of cinnamyl alcohol into the epoxide and cinnamaldehyde–benzaldehyde.

Therefore, we have also tested the vanadium–triazole complexes towards cinnamyl alcohol oxidation (see Fig. 21) [67]. The results obtained were compared with $VO(acac)_2$.

In acetonitrile $VO(acac)_2$ appears to be the most reactive catalyst. After 3 h, almost full conversion of the substrate is achieved and 17 turnovers towards the epoxide are obtained. The two vanadium–triazole complexes with ^{t}BuOOH yielded under those conditions only 1–2 turnovers into the epoxide and cinnamaldehyde [67]. In toluene the catalytic activities of the triazole-containing complexes were improved considerably approaching the values observed for the $VO(acac)_2$ complex (10–20 turnovers).

Although, due to the relatively low turnover numbers observed, we have not conducted mechanistic studies on the nature of these processes, some suggestions on the mechanism can be made. The commonly accepted reaction mechanism for epoxidation of allylic alcohols using the $VO(acac)_2$–^{t}BuOOH system involves binding of the substrate and alkylhydroperoxide to the V ion, after which oxygen transfer to the alkene takes place and subsequent dissociation of the alcohol and ^{t}BuOH allows further reactions [61,70]. As the turnover numbers of the triazole-containing complexes in acetonitrile are much lower than those observed for the $VO(acac)_2$ system, we infer that most of the complex remains intact. As the triazole-containing complexes yield relatively more cinnamylaldehyde versus epoxide (1:1) than the $VO(acac)_2$ system does (9:1), it is likely that the compounds themselves show the poor selectivity towards epoxide formation.

Using hydrogen peroxide as oxidant yielded in acetonitrile for the L^8-containing vanadium complex and $VO(acac)_2$ as catalysts turnover numbers of around 15, however, the selectivity is very poor (in both cases: epoxide:cinnamaldehyde:benzaldehyde 4:2:7). In toluene the $[VO_2L^9]^-$ complex and $VO(acac)_2$ catalysts give low turnovers into the epoxide (2 and 1 respectively) and cinnamaldehyde (1.5 and 1 respectively). The L9-containing complex does not yield any measurable amount of benzaldehyde, whilst under the same condition the $VO(acac)_2$ catalyst some benzaldehyde has been detected.

A poor selectivity indicates that hydroxyl radicals are involved in the catalysis. The observation that in toluene the activity is significantly lower than in acetonitrile could be explained by the fact that toluene traps the hydroxyl radicals better than acetonitrile does [71]. On other hand, LV(IV)–O–O* species as suggested by Mimoun and co-workers [45] or radical chain processes as inferred by Bonchio et al. based on their mechanistic studies [72], may also be operative in these oxidation processes.

9. Concluding remarks

In this contribution we have shown that vanadium complexes can yield a variety of oxidation reactions, both biomimetic (haloperoxidase activity) and non-biomimetic (epoxidation, alcohol oxidation, C=C cleavage, etc.). An important question, which remains open to be answered, is how to obtain vanadium complexes that are active as oxidation catalysts, give the desired selectivity, and show adequate stability under the conditions applied.

The stability and robustness of the complexes is particularly put to the test in functional models for vanadium bromoperoxidase, since these complexes have to be resistant to the harsh, acidic conditions necessary for the reaction to proceed. These conditions easily cause dissociation of the ligand from the vanadium centre and, therefore, often two or three oxygen donor sites are needed to afford the required stability.

Vanadium(V) species that are not coordinated to organic ligands already display a fairly high activity in bromination reactions. For example, *cis*-dioxovanadium(V) (VO_2^+) catalyses the bromination of TMB with a turnover rate of 15 mol TMBBr per mol vanadium h^{-1} [6]. Furthermore, most ligated functional model systems known in the literature only equal this activity, whereas V–BrPO functions with ca. 3000 times higher turnover numbers. Even the best mimic known until now, developed by Butler et al., appears to be only a slightly better catalyst than $VO(acac)_2$ [15]. Therefore, the search for a ligand system that provides a catalyst capable of approaching the enzyme in reaction rate and selectivity remains a difficult task. Obviously, the structural environment of the vanadate in the enzyme plays an important role in the catalytic process, so the

fact that the structure of the active site is now known in detail may facilitate the design of a catalyst which indeed approaches the reaction rates of the enzyme.

A real challenge remains the development of a vanadium catalyst capable of epoxidation of unfunctionalised olefins, since only low turnovers can be achieved with $VO(acac)_2$. Furthermore, research regarding vanadium-catalysed oxidation of alcohols to their corresponding aldehydes and ketones as well as hydroxylation reactions has remained highly underexposed.

Vanadium-catalysed epoxidations of allylic alcohols using *tert*-butylhydroperoxide (TBHP) are well known, since high yields are obtained and the reactions often proceed regioselective's [73–75]. Commercially available $VO(acac)_2$ is especially very appropriate for this purpose and is, therefore, often recommended as the catalyst [76,77]. High regioselectivities are a result of coordination of the allylic alcohol to the vanadium centre. Only vanadium complexes of bidentate ligands have the required vacant coordination sites for binding of the allylic alcohol and the peroxide in an μ^2 manner.

A thriving topic in vanadium chemistry is the search for chiral vanadium catalysts for the asymmetric epoxidation of allylic alcohols. Many effective systems have already been developed [78–83]. Moderate-to-high enantioselectivities and yields were reached in the allylic epoxidation of a range of disubstituted allylic alcohols using a *N*-bis(1-naphthyl)methyl-substituted hydroxamic acid [78]. Until now, the ligands used for asymmetric allylic epoxidations are mainly bulky hydroxamic acids, which are not easily accessible. In the near future the research will, therefore, certainly be focussed on the development of other, more simple, bulky bidentate ligands for the synthesis of vanadium epoxidation catalysts.

In recent years various promising vanadium catalysts have been reported for asymmetric sulfide oxidations [81–83]. These catalysts are excellent functional models of the vanadium peroxidases that also catalyse sulfoxidation reactions in an enantioselective fashion, as recently reported by ten Brink et al. [84]. High yields and enantioselectivities were reached with a limited number of substrates. The best results were reported using a Schiff base ligand derived from *tert*-leucinol [81–83]. In the asymmetric oxidation of *tert*-butyl disulfide, 98% conversion and 91% e.e. were reached. However, e.e's above 80% with simple sulfides like methyl phenyl sulfide have never been achieved. Future research in asymmetric vanadium-catalysed sulfoxidation chemistry should, therefore, be concentrated on the development of chiral vanadium complexes capable of oxidising a broader range of sulfide substrates.

Acknowledgements

This work was supported by Unilever Research and Development, Vlaardingen, The Netherlands.

References

[1] P.M. Geschwend, J.K. MacFarlane, K.A. Newman, Science 227 (1985) 1033.
[2] G.W. Gribble, Chem. Soc. Rev. 28 (1999) 335.
[3] R. Wever, W. Hemrika, in: J.O. Nriagu (Ed.), Vanadium in the Environment, Part One: Chemistry and Biochemistry (Chapter 12), Wiley, New York, 1998.
[4] A. Butler, Coord. Chem. Rev. 187 (1999) 17.
[5] R.R. Everett, J.R. Everett, A. Kanofsky, A. Butler, J. Biol. Chem. 265 (1990) 4908.
[6] A. Butler, in: J. Reedijk, E. Bouwman (Eds.), Bioinorganic Catalysis, 2nd ed (Chapter 5), Marcel Dekker, New York, 1999.
[7] A. Messerschmidt, R. Wever, Proc. Natl. Acad. Sci. USA 93 (1996) 392.
[8] A. Messerschmidt, L. Prade, R. Wever, Biol. Chem. 378 (1997) 309.
[9] M.N. Isupov, A.R. Dalby, A.A. Brindley, Y. Izumi, T. Tanabe, G.N. Murshudov, J.A. Littlechild, J. Mol. Biol. 229 (2000) 1035.
[10] M. Weyand, H.-J. Hecht, M. Kiess, M.-F. Liaud, H. Vilter, D. Schomburg, J. Mol. Biol. 293 (1999) 595.
[11] R. De La Rose, M.J. Clague, A. Butler, J. Am. Chem. Soc. 114 (1992) 760.
[12] F. Secco, Inorg. Chem. 19 (1980) 2722.
[13] C.L. Perrin, T.J. Dwyer, Chem. Rev. 90 (1990) 935.
[14] D. Crans, H. Holst, D. Rehder, Inorg. Chem. 34 (1995) 2524.
[15] M.J. Clague, N.L. Keder, A. Butler, Inorg. Chem. 32 (1993) 4754.
[16] G.J. Colpas, B.J. Hamstra, J.W. Kampf, V.L. Pecoraro, J. Am. Chem. Soc. 118 (1996) 3469.
[17] G.J. Colpas, B.J. Hamstra, J.W. Kampf, V.L. Pecoraro, J. Am. Chem. Soc. 116 (1994) 3627.
[18] A. Butler, M.J. Clague, in: H.H. Thorp, B.L. Pecoraro (Eds.), Mechanistic Bioinorganic Chemisty, p. 329, Adv. Chem. Ser. (1995) 246.
[19] A. Butler, A.H. Baldwin, in: P. Sadler, H.A.O. Hill, A. Thompson (Eds.), Structure and Bonding, vol. 89, 1997, p. 109.
[20] M.J. Clague, N.L. Keder, A. Butler, Inorg. Chem. 32 (1993) 4754.
[21] H. Sakurai, K. Tsuchiya, FEBS Lett. 260 (1990) 109.
[22] A.D. Keramidas, A.B. Papaioannou, A.T. Vlahos, T.A. Kabanos, G. Bonas, A. Makriyannis, C.P. Rapropoulou, A. Terzis, Inorg. Chem. 35 (1996) 357.
[23] A.T. Vlahos, E.I. Tolis, C.P. Raptopoulou, A. Tsohos, M.P. Sigalas, A. Terzis, T.A. Kabanos, Inorg. Chem. 39 (2000) 2977.
[24] C.R. Cornman, E.P. Zovinka, Y.D. Boyajian, K.m. Geiser-Bush, P.D. Boyle, P. Singh, Inorg. Chem. 34 (1995) 4213.
[25] A.T. Vlahos, T.A. Kabanos, C.P. Raptopoulou, A. Terzis, Chem. Commun. (1997) 269.
[26] T.A. Kabanos, A.D. Keramidas, A.B. Papaioannou, A. Terzis, J. Chem. Soc. Chem. Commun. (1993) 643.
[27] D. Rehder, Coord. Chem. Rev. 182 (1999) 297.
[28] D. Rehder, C. Schulzke, H. Dau, C. Meinke, J. Hanss, M. Epple, J. Inorg. Biochem. 80 (2000) 115.
[29] D.C. Crans, A.D. Keramidas, S.S. Amin, O.P. Anderson, S.M. Miller, J. Chem. Soc. Dalton Trans. (1997) 2799.
[30] M. Mahroof-Tahir, A.D. Keramidas, R.B. Goldfarb, O.P. Anderson, M.M. Miller, D.C. Crans, Inorg. Chem. 36 (1997) 1657.
[31] M. Bashirpoor, H. Schmidt, C. Schulzke, D. Rehder, Chem. Ber./ Recueil (1997) 651.

[32] W. Plass, Z. Anorg. Allg. Chem. 623 (1997) 461.
[33] R. Fulwood, H. Schmidt, D. Rehder, J. Chem. Soc. Chem. Commun. (1995) 1443.
[34] N. Julien-Cailhol, E. Rose, J. Vaisserman, D. Rehder, J. Chem. Soc. Dalton Trans. (1996) 2111.
[35] V. Vergopoulos, W. Priebsch, M. Fritzsche, D. Rehder, Inorg. Chem. 32 (1993) 1844.
[36] J.A. Martinez-Perez, M.A. Pickel, E. Caroff, W.-D. Woggon, Synlett 12 (1999) 1875.
[37] B.S. Hammes, V.G. Young, A.S. Borovik, Angew. Chem. Int. Ed. 38 (1999) 666.
[38] Z. Shirin, B.S. Hammes, V.G. Young, Jr., A.S. Borovik, J. Am. Chem. Soc. 122 (2000) 1836.
[39] C. Raposo, M. Almaraz, M. Martín, V. Weinrich, M.L. Mussóns, V. Alcázar, Chem. Lett. (1995) 759.
[40] W. Plass, Angew. Chem. Int. Ed. 38 (1999) 909.
[41] W. Hemrika, R. Renirie, H.L. Dekker, P. Barnett, R. Wever, Proc. Natl. Acad. Sci. USA 94 (1997) 2145.
[42] A. Ligtenbarg, Ph.D. thesis, University of Groningen, The Netherlands, 2001.
[43] M. de Loos, A.G.J. Ligtenbarg, J. van Esch, H. Kooijman, A.L. Spek, R. Hage, R.M. Kellogg, B.L. Feringa, Eur. J. Org. Chem. (2000) 3675.
[44] V.W. Day, W.G. Klemperer, A. Yagasaki, Chem. Lett. (1990) 1267.
[45] V. Conte, F. Di Furia, S. Moro, J. Phys. Org. Chem. 9 (1996) 329.
[46] A. Butler, M.J. Clague, G.E. Meister, Chem. Rev. 94 (1994) 625.
[47] H. Mimoun, L. Saussine, E. Daire, M. Postel, J. Fischer, R. Weiss, J. Am. Chem. Soc. 105 (1983) 3101.
[48] C.K. Sams, K.A. Jorgensen, Acta Chem. Scand. 49 (1995) 839.
[49] T. Itoh, K. Jitsukawa, K. Kaneda, S. Teranishi, J. Am. Chem. Soc. 101 (1979) 159.
[50] K.B. Sharpless, Chem. Tech. (1985) 692.
[51] H. Mimoun, M. Mignard, P. Brechot, L. Saussine, J. Am. Chem. Soc. 108 (1986) 3711.
[52] H. Mimoun, P. Chaumette, M. Mignard, L. Saussine, J. Fischer, R. Weiss, Nouv. J. Chim. 7 (1983) 467.
[53] M. Bonchio, V. Conte, F. Di Furia, G. Modena, Res. Chem. Intermed. 12 (1989) 111.
[54] W. Adam, D. Golsch, Chem. Ber. 127 (1994) 1111.
[55] F. Ballistreri, G.A. Tomaselli, R.M. Toscano, V. Conte, F. Di Furia, J. Am. Chem. Soc. 113 (1991) 6209.
[56] G.B. Shul'pin, D. Attanasio, L. Suber, J. Catal. 142 (1993) 147.
[57] I.I. Moiseev, A.E. Gekhman, D.I. Shishkin, New J. Chem. 13 (1989) 683.
[58] O. Bortolini, V. Conte, F. Di Furia, G. Modena, Nouv. J. Chim. 9 (1985) 147.
[59] V. Conte, F. Di Furia, G. Modena, J. Org. Chem. 53 (1988) 1665.
[60] O. Bortolini, V. Conte, F. Di Furia, G. Modena, Nouv. J. Chim. 9 (1985) 147.
[61] V. Conte, F. Di Furia, G. Licini, Appl. Cat. A 157 (1997) 335.
[62] A.G.J. Ligtenbarg, A.L. Spek, R. Hage, B.L. Feringa, J. Chem. Soc. Dalton Trans. (1999) 659.
[63] R. Hage, J.G. Haasnoot, J. Reedijk, R. Wang, E. Ryan, J.G. Vos, A.L. Spek, A.J.M. Duisenberg, Inorg. Chim. Acta 174 (1990) 77.
[64] J.G. Haasnoot, Coord. Chem. Rev. 200 (2000) 131.
[65] J.G. Vos, Polyhedron 11 (1992) 2285.
[66] F. Barigelletti, L. De Cola, V. Balzani, R. Hage, J.G. Haasnoot, J. Reedijk, J.G. Vos, Inorg. Chem. 28 (1989) 4344.
[67] A.G.J. Ligtenbarg, R. Hage, F. Hartl, T. Mahabiersing, M. Lutz, A.L. Spek, B.L. Feringa, Dalton (2001), to be submitted to Inorg. Chim. Acta.
[68] H. Hefele, E. Uhlemann, F.Z. Weller, Naturforsch 52b (1977) 693.
[69] A.S. Ceccato, A. Neves, M.A. De Brito, S.M. Drechsel, A.S. Mangrich, R. Werner, W. Haase, A.J. Bortoluzzi, J. Chem. Soc. Dalton Trans. (2000) 1573.
[70] A.O. Chong, K.B. Sharpless, J. Org. Chem. 42 (1977) 1587.
[71] G. Roelfes, M. Lubben, R. Hage, L. Que, Jr., B.L. Feringa, Chem. Eur. J. 6 (2000) 2152.
[72] M. Bonchio, V. Conte, F. Di Furia, G. Modena, S. Moro, J. Org. Chem. 59 (1994) 6262.
[73] H.E.B. Lempers, A. Ripollés i Garcia, R.A. Sheldon, J. Org. Chem. 63 (1998) 1408.
[74] S. Tanaka, H. Yamamoto, H. Nozaki, K.B. Sharpless, R.C. Michaelson, J.D. Cutting, J. Am. Chem. Soc. 96 (1974) 5254.
[75] K.B. Sharpless, R.C. Michaelson, J. Am. Chem. Soc. 95 (1973) 6136.
[76] L.A. Paquette (Ed.), Encyclopedia of Reagents for Organic Synthesis, Wiley, Chichester, 1995, p. 8.
[77] K.C. Nicolaou, E.J. Sorensen, Classics in Total Synthesis (Chapter 34), VCH, Weinheim, 1996.
[78] Y. Hoshino, H. Yamamoto, J. Am. Chem. Soc. 122 (2000) 10452.
[79] Y. Hoshino, N. Murase, M. Oishi, H. Yamamoto, Bull. Chem. Soc. Jpn. 73 (2000) 1653.
[80] N. Murase, Y. Hoshino, M. Oishi, H. Yamamoto, J. Org. Chem. 64 (1999) 338.
[81] D.A. Cogan, G. Liu, K. Kim, B.J. Backes, J.A. Ellman, J. Am. Chem. Soc. 120 (1998) 8011.
[82] C. Bolm, F. Bienewald, Synlett (1998) 1327.
[83] C. Bolm, F. Bienewald, Angew. Chem. Int. Ed. Engl. 34 (1995) 2640.
[84] H.B. ten Brink, A. Tuynman, H.L. Dekker, W. Hemrika, Y. Izumi, T. Oshiro, H.E. Schoemaker, R. Wever, Inorg. Chem. 37 (1998) 6780.